COATED IMPLANTABLE MEDICAL DEVICE

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CLAIMS

[Claim(s)]

1. This Structure (12) Has at Least One Field Here with Structure (12) suitable for Inserting in Patient's Inside of the Body. It consists of base materials (14). At least one enveloping layer arranged on one field of said structure (12) (16), It has at least one layer of the 1st biological active substance of said at least one enveloping layer (16) arranged upwards in part at least. Said at least one enveloping layer (16) is an implantable medical device characterized by what is emitted at the rate by which said biological active substance was controlled from said at least one enveloping layer (16) (10).

2. It is the instrument according to claim 1 which it has further at least one porous layer (20) arranged on said biological active substance layer (18), and said at least one porous layer (20) consists of polymers, and is characterized by emitting said polymer at the rate by which said biological active substance was controlled through said at least one porous layer (10).

3. Said at least one enveloping layer (16) is an instrument according to claim 1 characterized by containing the nonporous matter or a parylene derivative (10).

4. The thickness of said at least one enveloping layer (16) is an instrument according to claim 3 which is within the limits of 50,000-500,000A, and is characterized by being within the limits of 100,000-500,000A, and being about 200,000A most preferably (10).

5. Said nonporous matter is an instrument according to claim 3 of the adsorbent matter and absorbents which have about 230,000A thickness preferably which comes out on the other hand at least, and is characterized by a certain thing (10).

6. Said biological active substance layer is an instrument according to claim 1 characterized by containing an anti-platelet GP IIb/IIIa antibody (10).

7. Said biological active substance layer is an instrument according to claim 1 characterized by containing a desirable chimera monoclonal antibody like an anti-platelet GP IIb/IIIa antibody (10).

8. Said at least one porous layer (20) is an instrument according to claim 1 characterized by carrying out a polymerization from a non-catalyst monomer steam (10).

Said Biological Active Substance 9. Heparin, Covalent-Bond Heparin, or Another Thrombin Inhibitor, Hirudine, a leech log, argatroban, D - Phenyl alanyl-L-Polly L-arginyl chloro methyl ketone, Or another anti-thrombon formation medicine or such mixture; Urokinase, Streptokinase, an organization plasminogen activator, or another thrombolysis medicine, or such mixture; -- fibrinolysis medicine; -- vasospasm inhibitor and calcium channel blocker -- The antihypertensive drug; antimicrobial drug or antibiotic of a nitrate, nitrogen oxide, a nitrogen oxide promoter, another vasodilator;Hytrin (trademark), or others; Aspirin, Ticlopidine, glycoprotein IIb/IIIa inhibitor, another inhibitor of a surface glycoprotein acceptor, or another platelet inhibitor; A colchicine, another antimitotic, or another microtubule inhibitor, Dimethyl sulfoxide (DMSO), a retinoid, or another anti-secretion medicine; cytochalasin or another actin inhibitor; Or RIMODE ring inhibitor; The another drugs; methotrexate or another antagonism-inhibitor for a deoxyribonucleic acid, an antisense nucleotide, or a molecule heredity break in, or anti-growth medicine; tomoxifen SHITORETO, Taxol (trademark), this derivative, or other anticancer chemotherapeutic drugs; Dexamethasone, A dexamethasone-sodium-phosphate salt, dexamethasone acetate, another dexamethasone derivative, another anti-inflammation steroid, a non-steroidal anti-inflammatory drug; cyclosporine, or another immunosuppressive agent; TORAPIDARU (PDGF antagonist), ANGIOPEPUCHIN (growth hormone antagonist), ANGIO genin, a growth factor, an anti-growth factor antibody, or another growth factor antagonist; Dopamine, The bromocriptine mesylate, the pel GORAIDO mesylate, or another dopamine agonist;60Co (half-life 5.3 years), 192Ir(s) (half-life 73.8 days), 32P (half-life 14.3 days), 111In (half-life 68 hours), 90Y (half-life 64 hours), 99mTc (half-life 6 hours), or another radiotherapy medicine; An iodine content compound, Another heavy metal which functions as a bromine content compound, gold, a tantalum, platinum, a tungsten, or a radiopacity agent; A peptide, Protein, an enzyme, an extracellular stromata component, a cell component, or another biological drugs; Captopril, Enalapril or another angiotensin converting enzyme (ACE) inhibitor; An ascorbic acid, The alpha-

tocopherol, a superoxide dismutase, deferoxamine, 21-amino steroid (Lasa Lloyd), or another free radical scavenging medicine, iron chelating agent or antioxidizing medicine; -- the indicator was carried out with the radioisotope of 14C, 3H, 131I, 32P, or 36S -- or which above drugs; estrogen, another sex hormone;AZT, or others of another form by which the radioisotope indicator was carried out -- anti- -- polymerase; aciclovir -- Famciclovir, a rimantadine hydrochloride, ganciclovir sodium, NORUBIRU, Crixivan, or other antiviral drugs; 5-aminolevulinic acid, A meta-tetra-hydroxyphenyl chlorin, a hexa deca fluoro zinc phthalocyanine, Tetramethyl hematoporphyrin, a rhodamine 123, or another photodynamics remedy ;P A seudomonas aeruginosa exogenous toxin is opposed. A431 EPIDEROMOIDO cancer cell and a reactant IgG2 kappa (kappa) antibody, Remedy; gene therapy medicine aiming at the monoclonal antibody which opposes the noradrenalin enzyme dopamine beta-hydroxylase which carried out covalent bond to saporin, or other antibodies; enalapril and other prodrugs;
Or the instrument according to claim 1 characterized by containing at least one of which such mixture (10).
10. It is Instrument (10) According to Claim 1 with which it Has Further at Least One Adhesion Acceleration Layer (30) Arranged on One Field of Structure (12), and Said Enveloping Layer (16) is Characterized by Thing of Said Adhesion Acceleration Layer (30) for which Part is Arranged Upwards at Least.

[Translation done.]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
Name of invention Covered implantable medical device detailed-description technical field
Generally this invention relates to the medical device for Homo sapiens and veterinarians. Furthermore, this invention relates to a detail at a drug or the medical device which incorporated activity drugs biologically.
Background technique It is becoming general by transplanting an implantable medical device to the location of others of the inside of the body of an esophagus, a trachea, a large intestine, a bile duct, a ureter, the circulatory system, Homo sapiens, or a brute patient altogether selectively to treat various medical conditions. For example, under many therapies of the circulatory system, installation of instruments, such as stent, a catheter, balun, a wire guide, and cannula, is needed. However, when such an instrument is introduced in the circulatory system and operated through this circulatory system, a blood vessel wall is disturbed and it is damaged. In this injury part, clot-of-blood formation or thrombosis often arises, consequently the constriction of a blood vessel or lock out takes place. Furthermore, if such a medical device is saved by a patient's inside of the body over a long period of time, it will often be generated in the medical device itself, and thrombosis will cause a constriction or lock out as a result. Consequently, a patient is put to the risk of various complication (for example, a heart stroke, versicular emphysema, apoplexy, etc.). Therefore, the activity of such a medical device connotes the danger in question of having planned to have improved the activity.
A blood vessel depends another gestalt which wears a constriction on a disease. Probably, the universal disease that starts the constriction of a blood vessel is atherosclerosis. Atherosclerosis is a disease which generally does an adverse effect to a left gastric artery, a main artery, an ilium femur artery, and a carotid artery. A lipid, fibroblast, and the atheroma nature plaque (spots) of a fibrin increase, and lock out of an artery is caused. The critical level of a constriction reaches even the point that the blood flow which passes through a lock out part becomes inadequate for filling the metabolic turnover initial complement of the organization by the side of the down-stream distance of a lock out part as lock out advances. Consequently, it becomes the ischemia.
For the treatment of atherosclerosis, many medical devices and the therapy approaches are learned. Especially an example of a useful cure of a certain kind of atherosclerosis lesion is a percutaneous transluminal cavity angioplasty (PTA). During a PTA operation, the catheter with which balun was attached at the head is inserted into a patient's artery. In this case, balun is contracted. The head of a catheter is advanced even in the part of the atherosclerosis plaque which should be expanded. Arrange balun in the constriction area of an artery, or intersect this area, and it is made to arrange, and is made to expand after that. expansion of balun -- an atherosclerosis plaque -- " -- it is broken, "and a blood vessel are expanded and a constriction is eased selectively thereby at least.
Although PTA is used widely now, two big problems exist in this. A blood vessel receives [1st] acute lock out immediately after several hours within several hours of the beginning after extended treatment. Such lock out is called "burst nature closeout." When it happens to about 5% of the case for which PTA is used and a blood flow is not recovered immediately, burst nature

closeout starts myocardial infarction and dies. It is thought that the main devices of burst nature closeout are elastic counteraction, the overhaul of an artery, and/or thrombosis. If an artery wall is directly medicated with suitable drugs (for example, antithrombin agent) when performing an angioplasty, although considered, the result of the attempt for which the incidence rate of thrombus nature acute closeout can be reduced and which is such direct administration will get confused, and it will not be [a result] ascertained.
The 2nd main problem which encounters in PTA is that an artery becomes narrow again after the first successful angiogenesis. this -- again -- ****** -- things are called the "restenosis" and, generally happen within six months of the beginning after angiogenesis. It is thought that the restenosis is based on growth and shift of the cell component from an artery wall, and also it is generated by the geometry change in artery Kabeuchi called "a RIMODE ring (remodeling)." With it being the same, if an artery wall is directly medicated with suitable drugs, it is thought that the cell and/or RIMODE ring event which cause the restenosis are checked. However, the result of the attempt which controls the acute closeout by the thrombus, and the attempt which controls the restenosis by this approach similarly also gets confused, and it is not ascertained.
The vasoconstriction by non-ADEROMU sclerosis can also be treated by PTA. For example, TAKAYASU arteritis or the neurofibromatosis causes the constriction by the fibrosing disease nature thickening of an artery wall. However, the restenosis of these lesions is generated at a high rate after the operation [angiogenesis] with the fibrosing disease-property of a disease. Similarly a therapy or the medicine therapy to prevent does not have effectiveness in these.
An instrument like the stent in a vessel is the useful add-on to PTA. It is add-on useful in the closeout which may take place especially acute [of an angiogenesis after the operation], or in the future. In order to prevent sudden closeout and the restenosis mechanically, the stent is arranged in the amplification area of an artery. Even if it uses stent transplantation together to offensive and unluckily exact the antiplatelet and an anticoagulant therapy (for example, systemic administration), the incidence rate of thrombosis nature blood vessel closeout or other thrombosis complication is not successful until now [high], so that prevention of a **** and the restenosis is expected. furthermore, ** of a systemic antiplatelet therapy and a systemic anticoagulant therapy -- since better, when the most, it passes through a colander side effect and it is the high incidence rate of the bleeding complication in a vessel penetration part.
the stent and catheter with which other conditions and diseases are inserted in the part of others of an esophagus, a trachea, a large intestine, a bile duct, a ureter, and the inside of the body, cannula, and other instruments -- or it can treat with orthopedic equipments, the implant, or an alternative.
In order to treat or prevent such a condition and a disease, for example, in order to prevent the burst nature closeout and/or the restenosis for the interior of the body like a path, a lumen, or a blood vessel, the midst or the drugs suitable after that for a predetermined part in the living body of medical treatment, a drug or the instruments for prescribe the activity matter for the patient with high dependability directly biologically, and development of an approach are desire. as a concrete case -- PTA -- or while [, such as atherectomy (atherectomy) and laser excision,] it is another, to develop the instruments and approach of medicating with the drug of an antithrombin agent or others the part of the blood vessel treated by ****** is desired.
Moreover, as for such instruments, it is desirable to pass into the possession of the both sides of a long period of time (namely, after a therapy, for several weeks and several months) at a short (namely, for several after [a therapy] hours of the beginning and, and several days) list, and to prescribe these drugs for the patient. Moreover, it is desirable drugs, a drug or to control the administration rate of the activity matter to accuracy biologically, and to restrict whole body exposure to these drugs. Especially in a cure including medicating a specific organ or a specific part with a chemotherapic drug with an intravenous catheter (there being an advantage which mitigates the amount of drugs which needs this very thing for a therapy without something to say) by preventing both constrictions [in / it reaches and / a catheter head] that met the catheter, it is useful. Various cures for other are improvable similarly. the inside of the nest of such [that it is needless to say and] instruments -- or it is also desirable the drugs in such instruments, a drug, or to avoid disassembly of the activity matter biologically.

Outline of invention The aforementioned problem is solved by the vessel stent of this invention, or other implantable instruments, and technical progress is acquired. The vessel stent of this invention or other implantable instruments are emitted to the part of others of the vessel by which this stent or instruments are arranged, its alien system, or the inside of the body at drugs, a drug, or the rate by which the activity matter was controlled biologically. this invention persons discovered that disassembly of the activity matter was biologically avoidable the drugs used for such instruments, a drug, or by arranging an enveloping layer in one front face of the instrument structure. Drugs, a drug, or the matter [activity / target / biology] is arranged on [some] an enveloping layer at least. This enveloping layer is emitted at the rate which has been arranged on this enveloping layer and by which the activity matter was controlled biologically. Furthermore, the medical device of this invention also has further the porous layer biologically arranged on the activity matter. This porous layer consists of polymers and this polymer is emitted at the rate by which the activity matter was biologically controlled through the porous layer.
An enveloping layer consists of a nonporous ingredient of for example, a parylene (parylene) derivative in a certain embodiment. The thickness of this enveloping layer is within the limits of 50-500,000A (henceforth "A") preferably, and is within the limits of 100,000-500,000A much more preferably. Specifically, it is about 200,000A. In the another embodiment, a nonporous ingredient is an adsorbent or an absorbent and the thickness of the enveloping layer of an adsorbent or an absorbent is about 230,000A.
In the another embodiment of this invention, the layer of the activity matter contains a chimera monoclonal antibody like an antiplatelet GPIIb/IIIa antibody biologically.
In the still more nearly another embodiment of this invention, the adhesion acceleration layer is arranged on the 1 front face of the instrument structure, and an enveloping layer is arranged upwards, even if [a part of] there are few these adhesion acceleration layers.
Preferably, as for an adhesion acceleration layer, thickness includes the silane of 0.5-5,000A within the limits. Moreover, being avoided by covering drugs, a drug, or a biological active substance with the porous layer of the biocompatibility polymer applied without using the chemical or technique of the solvent and catalyst which tend to disassemble or damage these drugs, a drug, or a biological active substance, heat, or others also discovered disassembly of the drugs with which this invention persons were applied to such an instrument, a drug, or a biological active substance. Preferably, these biocompatibility polymers are applied by vacuum evaporationo or plasma vacuum evaporationo, and from a vacuum evaporationo layer, the polymerization of them is carried out by mere condensation, and they are stiffened, or carry out a polymerization in photolysis. It is thought that a biocompatibility polymer is useful for this object. However, needless to say, the other coat approaches can also be used.
When it is for this instrument to use it by the circulatory system, as for an inner biological active substance, it is much more desirable that they are heparin, another anti-crystal plate matter, an antithrombin agent or dexamethasone, dexamethasone acetate, a dexamethasone-sodium-phosphate salt, another dexamethasone derivative, or an anti-inflammatory steroid at least. Furthermore, the biological active substance of other extensive classes can be used. For example, they are :thrombolysis agent which is not limited only to these although the drugs of the following categories can be used, vasodepressor, an anti-hypertension agent, an antimicrobial agent, an antibiotic, an antimitotic agent, an anti-growth agent, an anti-secretion agent, a non steroid anti-inflammatory agent, an immunosuppresant, a growth factor, a growth factor antagonist, an antitumor agent and/or a chemotherapic drug, anti-polymerase, an antivirotic a photodynamics therapy agent, an antibody target therapy agent, a prodrug, a sex hormone agent, a free radical scavenger, an antioxidant, a biological, a radiotherapy agent, a radiopacity agent, and a radioisotope indicator agent. The main constraint is that this biological active substance must be able to bear the vaccum pressure used during spreading technique, for example, vacuum evaporationo of at least one porous layer, or plasma vacuum evaporationo. If it puts in another way, a biological active substance must have comparatively low vapor pressure in vacuum evaporationo temperature (generally a room temperature or temperature near a room temperature).
As for at least one porous layer, it is desirable to consist of the polyamides, the parylenes, or

the parylene derivatives which were applied by non-catalyst vacuum evaporationo. Moreover, it is convenient that it is the thickness of about 5,000 to 250,000 A, and if it is this thickness, it can emit at the rate by which the biological active substance was controlled. Although "parylene" means both the generalization name of the known polymer group generated by the vapor-phase-polymerization method on the basis of para xylene, and the name of the unsubstituted object of this polymer, on these descriptions, it is used in the sense of the latter. Furthermore, first, parylene or a parylene derivative heats para xylene or a suitable derivative at suitable temperature (for example, about 950 degrees C), and, specifically, is manufactured by generating the G para xylene (or this derivative) of an annular dimer. The obtained solid can be isolated in a pure form.

Subsequently, this solid is disassembled or pyrolyzed at suitable temperature (for example, about 680 degrees C), and the monomer steam of para xylene is generated. This monomer steam is cooled even to suitable temperature (for example, 50 degrees C or less), and it is made to condense on a desired body (for example, at least one layer of a biological active substance). The obtained polymer has the repeat unit of -(-CH2C6H4CH2-) n-. Here, n is about 5,000 and molecular weight is within the limits of 500,000.

As mentioned above, having various biomedical applications is known and the parylene and the parylene derivative coat which can be applied with vacuum deposition are marketed from various contractors. For example, it is marketed from Special Coating Systems (100 Deposition Drive, Clear Lake, and WI 54005), Para Tech Coating, Inc. (35 Argonaut, Aliso Viejo, CA 92656) and Advanced Surface Technology, Inc. (9 Linnel Circle, Billerica, MA 01821-3902), etc.

At least one porous layer can be applied also by plasma vacuum evaporationo as another method. The plasma is ionization gas which is maintained in a vacuum and excited by electric energy (generally electric energy of a RF region). Since gas is maintained in a vacuum, plasma vacuum evaporationo processing is performed at the temperature a room temperature or near a room temperature. The plasma can be used for vapor-depositing polymers, such as silicon besides a polymer like Pori (ethylene oxide), Pori (ethylene glycol), and Pori (propylene oxide), methane, tetrafluoroethylene (for example, the polymers shown by trademark called Teflon), and tetramethyl disiloxane.

Although the aforementioned explanation shows some of the desirable embodiments of this invention, other polymer systems can also be used. For example, the polymers guided from a photopolymerization system monomer can be used. Moreover, for example, the spreading technique of others, such as immersion and fuel spray, can also be used.

The medical device of this invention can also have the layer of a biological active substance which is different in the crowning of the structure more than two-layer. However, generally on the front face where the instruments in the same layer differ for the object of this invention, the same biological active substance is not arranged. If it puts in another way, each front face of the instrument structure will wear a different biological active substance except for the case where a biological active substance is an innermost layer or an outermost layer of drum. For example, heparin can form an innermost layer, an outermost layer of drum, or both layers. These additional layers are also separable by also being able to make it arrange directly mutually at the topmost part, or arranging an additional porous layer between each class. Furthermore, a biological active substance layer can also consist of mixture of a different biological active substance. Moreover, as for a porous layer, it is desirable to consist of parylene or a parylene derivative. In a convenient thing, two or more biological active substances can have different solubility. Therefore, as for the layer containing the biological active substance (for example, dexamethasone) of low solubility, it is desirable to make it arrange on the layer containing the biological active substance (for example, heparin) of high solubility. Without expecting, this configuration raised some bleedoff-comparatively rates in the test tube of a refractory like dexamethasone, and some things like heparin for which the bleedoff rate of the soluble matter is reduced comparatively were discovered simultaneously.

Although the structure contained in an instrument can be formed by various approaches, as for this structure, it is desirable to be formed as vessel stent which consists of biocompatibility metals, such as a stainless steel, nickel, silver, platinum, gold, titanium, a tantalum, iridium, a

tungsten, Nitinol (Nitinol), and Inconel (Inconel). Thickness can also arrange the in general nonporous additional enveloping layer of the parylene of about 50,000 to 500,000 A, a parylene derivative, or other biocompatibility polymers directly just under the crowning of the vessel stent, and at least one biological active substance layer. Although an additional enveloping layer must be the thing of comparatively low ****, it is nonporosity in general, i.e., in an anticipated-use environment, it is more desirable than at least one porous layer that it is the nonporosity of sufficient like to make the stent into impermeability in general to blood.
The instrument and approach of this invention are useful also as the bottom of about [being useful although it is used in the locations where the inside of the body of an esophagus a trachea, a bile duct, a ureter and Homo sapiens like the circulatory system, or the patient of a brute is various], and a dura mater and orthopedic equipments, implant, or alternatives. The instrument and approach of this invention are useful especially although the midst of the treatment in a vessel or the back is certainly medicated with a suitable biological active substance. Moreover, it was discovered that the instrument and approach of this invention are useful especially although sudden closeout and/or the restenosis of a blood vessel are prevented. Furthermore, the instrument and approach of this invention can medicate a detail with an antithrombin agent, the antiplatelet, an anti-inflammatory steroid, or other drugs in the vascular area region opened for example, by the PTA method. Similarly, the instrument and approach of this invention can medicate the lumen of a blood vessel with a certain biological active substance, and can medicate a blood vessel wall with another biological active substance. By using a porosity polymer layer, the bleedoff rate of a biological active substance is carefully controllable about a short period of time and prolonged both sides.
These embodiments of this invention and other embodiments will be correctly recognized by this contractor, if you read and understand the publication of this description.
You combine a biological active substance with a nonporous layer, and make it eluted with sufficient convenience over a very long period in the another embodiment of this invention. This nonporous layer is combined with the base material of the structure. A nonporous layer can use the matter of arbitration which it can form from the matter of arbitration which is enumerated above and enumerated below, and biological active substances are enumerated above similarly, and is enumerated below. being convenient -- moreover, in the desirable embodiment, a glycoprotein IIb/IIIa inhibitor like commercial ReoPro (trademark) is combined with the nonporous layer of the parylene arranged in the outside surface of a medical device like the coronary artery stent. In a convenient thing, ReoPro (trademark) is eluted from the front face of the stent over a very long period.
Easy explanation of a drawing Drawing 1 is the sectional view of the 1st desirable embodiment of this invention.
Drawing 2 is the sectional view of another desirable embodiment of this invention.
Drawing 3 is the sectional view of still more nearly another desirable embodiment of this invention.
Drawing 4 is the sectional view of an embodiment with still more desirable others of this invention.
Drawing 5 is the sectional view of the additional desirable embodiment of this invention.
Drawing 6 A-6B is the sectional view of the additional desirable embodiment of this invention.
Drawing 7 is the sectional view of the additional desirable embodiment of this invention.
Drawing 8 is the partial amplification top view of drawing 7 .
Drawing 9 is the expanded sectional view which met nine to 9 line of drawing 8 .
Drawing 10 A-10D is the expanded sectional view which met ten to 10 line of drawing 8 .
Drawing 11 is the sectional view of another embodiment of the medical device of drawing 1 which uses the polymer enveloping layer with which the biological active substance was combined.
Drawing 12 is the sectional view of still more nearly another embodiment of the medical device of drawing 11 which the polymer enveloping layer pasted up on the outside surface of the base material of an instrument using the adhesion acceleration layer.
Detailed description Drawing 1 is referred to. Drawing 1 shows the implantable medical device 10

by this invention. This medical device 10 consists of the structure 12 which was suitable for inserting in the inside of the body of Homo sapiens or the patient of a brute first. It means that the structure 12 "which was suitable" has the configuration and magnitude for such insertion. A part of structure 12 is shown in drawing 1 for clarification.
As an example, the structure 12 is formed as vessel stent suitable for especially inserting in a patient's circulatory system. however, this stent structure -- an esophagus, a trachea, a large intestine, a bile duct, an urethra, and a ureter -- and -- especially -- a dura mater -- it can also be used by the system and part of following others. As an exception method, the structure 12 can also be formed as a vessel in ordinary use or other medical devices, and can actually contain the add-on of others, such as stent of various daily use or a strand wound spirally, and a dotting punch cylinder. Furthermore, since the trouble raised by this invention happens to the patient inside of the body about these parts of the instrument arranged actually, the structure 12 inserted does not need to be the whole instrument and it can also be some instruments of the vessel planned or others to be inserted in the patient inside of the body. Therefore, the structure 12 can be formed as at least one piece or these parts of a catheter, a wire guide, cannula, the stent, a vessel or other transplants, coronary artery pace maker lead wire or a lead-wire chip, coronary artery defibrillator lead wire or a lead-wire chip, a heart valve or an orthopedics instrument, an appliance, the implant, or the alternatives. Moreover, the structure 12 can also be formed as combination of some parts of ones of these things.
However, as for the structure 12, it is also most desirable to form as vessel stent like Gianturco-Roubin FLEX-STENT (trademark) marketed from Cook Incorporated, Bloomington, and Indiana or the GR II (trademark) coronary artery stent.
Generally, die length is about 10 - 60mm of abbreviation, and when inserted in a patient's circulatory system, such stent is designed so that it may be extended even to the diameter of about 2 - 6mm of abbreviation. Generally, die length is about 12 - 25mm of abbreviation, and when inserted, especially the Gianturco-Roubin stent is designed so that it may be extended to the diameter of about 2 - 4mm of abbreviation.
Needless to say, these stent dimensions are applicable to the typical stent used by the coronary artery stent. The structure like the stent which it is going to use at least inside the body of everybody but a patient like a main artery, an esophagus, a trachea, a large intestine, a bile duct, or a ureter, or a catheter part has a different dimension which was further suitable for such an application. For example, a main artery, an esophagus, a trachea, and the stent for large intestines can also have the diameter of about 25mm or less, and die length of about 100mm or more.
The structure 12 consists of suitable base materials 14 for the application for which the structure 12 was planned. As for a base material 14, it is desirable that it is biocompatibility. However, cell damage nature or other poisonous base materials can also be used if these are appropriately isolated from a patient. Such a biocompatible mater is useful in the radiotherapy which arranges the radioactive substance with the specific in-house which should be treated, or the catheter near an organization, for example. However, when the most, the base material 14 of the structure 12 must be biocompatibility.
The ingredient of various daily use can be used as a base material 14. Some ingredients are much more useful about the structures other than the coronary artery stent which is the example of a type of the structure 12. A base material 14 can also be elasticity or inelastic any according to the flexibility of a polymer layer or elasticity which should be applied on a base material. Base materials can also be any of biodegradability or non-biodegradability, and its various biodegradability polymers are well-known. Furthermore, though some biologicals are not useful especially in the typical coronary artery stent, it has sufficient reinforcement to function as a base material 14 of some useful structures 12.
A base material 14 Therefore, a stainless steel, a tantalum, titanium, Nitinol, Which [gold, platinum, Inconel, iridium, silver a tungsten, another biocompatibility metals, or / these] alloy; carbon or carbon fiber; Cellulose acetate, A cellulose nitrate, silicon, polyethylene terephthalate, polyurethane, A polyamide, polyester, poly orthochromatic ester, a polyacid anhydride, polyether sulphone, A polycarbonate, polypropylene, the amount polyethylene of giant molecules,

polytetrafluoroethylene, Or another biocompatibility polymeric materials, such mixture, or these copolymers; Polylactic acid, Polyglycolic acid or these copolymers, a polyacid anhydride, the poly caprolactone, Polyhydroxy butyrate valerianate, another biocompatibility polymers, such mixture, or these copolymers; Protein, At least one of an extracellular stromata component, a collagen, a fibrin, another biological;, or which [these] suitable mixture can be included. When the structure 12 is formed as vessel stent, especially as a base material 14, a stainless steel is useful.
When the structure 12, needless to say, consists of polypropylene, polyethylene, or roentgenoparent matter like said other polymers, it is desirable to apply a roentgenopaque coat in ordinary use to this structure 12. A roentgenopaque coat offers a means to identify the location of the structure 12 by the X-ray or the fluoroscope during insertion to a patient's circulatory system, or after insertion.
Drawing 1 is referred to further. Next, the vessel instrument 10 of this invention has at least one layer 18 of the biological active substance arranged on one front face of the structure 12. or [that arrange at least one biological active substance on one front face of the structure 12 for the object of this invention, and the front face of another side does not have a biological active substance] -- or it has one or more different biological active substances. Thus, measures which can prescribe one or more biological active substances or drugs for the patient into a blood flow from the lumen side of the stent for example, by the vessel stent, and are different in them can be taken against the tubing front face of the stent. Even if the selected matter is exposed to the vacuum lengthened during vacuum evaporationo or plasma vacuum evaporationo, as long as it can remain, a very extensive drug, drugs, and the matter can be used as a biological active substance in a layer 18. It is the matter which prevents or improves the acute closeout and the restenosis of a blood vessel by which especially the useful thing was opened in advance by the stent interposition operation or other treatment although this invention is carried out.
When the structure 12 is the vessel stent, especially useful biological active substances are a thrombolysis (thrombus is made to dissolve, decompose or dissipate) agent, and (generation of a thrombus is checked or prevented) an anti-thrombogen formation agent. Especially desirable thrombolysis agents are urokinase, streptokinase, and an organization plasminogen activator. Especially desirable anti-thrombogen formation agents are heparin, a leech bottle, and the antiplatelet.
Generally urokinase is plasminogen activating enzyme obtained from a human kidney cell culture object. Urokinase carries out the catalyst of the conversion to the fibrinolysis nature plasmin (this is decomposed to fibrin TOROMBI) of plasminogen.
Generally heparin is the anticoagulant of the mucopolysaccharide obtained from the intestinal mucosa of Buta, or the lungs of a cow. Heparin functions as a thrombin inhibitor by raising an operation of the endogenous antithrombin III of blood substantially. The thrombin which is a powerful enzyme in a coagulation cascade is an important point at the time of carrying out the catalyst of the generation of a fibrin. Therefore, heparin checks generation of a fibrin thrombin by checking a thrombin. As an exception method, covalent bond of the heparin is carried out in the outer layer of the structure 12. Therefore, the outermost layer of drum of the structure 12 is generated, and it is not easily decomposed by the enzyme, but heparin holds the activity as a thrombin inhibitor.
Needless to say, the biological active substance which has other functions can also be prescribed for the patient with the sufficient result with the instrument 10 of this invention. For example, an anti-growth agent like methotrexate checks superfluous growth of a smooth muscle, therefore checks the restenosis like the extension of a blood vessel. As for an anti-growth agent, it is desirable to be supplied over the period of about four - six months for this object. Furthermore, local administration of an anti-growth agent is also useful although various malignant conditions characterized by high vessel growth are treated. In such a case, the instrument 10 of this invention can be arranged in artery supply of a neoplasm, and a means to medicate a neoplasm with the anti-growth agent of a high dose directly comparatively can be offered.
Calcium channel blocker or a vasodilator like a nitrate controls vasospasm. Vasospasm happens universally after an angiogenesis operation. Vasospasm is generated as a response to breakage

on a blood vessel. Moreover, the inclination to start vasospasm falls according to recovery of a blood vessel. Therefore, as for a vasodilator, it is desirable to supply over the period for about two - three weeks. Needless to say, the traumatic failure by the angioplasty is not only the vascular injury which can start vasospasm. Moreover, an instrument 10 can be inserted in the circumference artery for preventing the vasospasm in vessels other than a coronary artery, for example, a main artery, a carotid artery, a renal artery, an iliac artery, or an artery etc.
When the structure 12 is formed in things other than the coronary artery stent, especially other various biological active substances are suitable for those applications. For example, a local neoplasm can be medicated with an anticancer chemotherapic drug with an instrument 10. Furthermore, a detail can be medicated with a rear spring supporter and drugs to a neoplasm at a long period of time with a comparatively high dose, arranging an instrument 10 to the inside of the artery which supplies blood to a neoplasm, or the part of arbitration, and reducing whole body exposure and toxicity. before an operation [to which these drugs reduce the magnitude of a neoplasm / for a therapy] -- it can be DEBARUKA (debulker) or can also be palliative which mitigates the symptom of a disease. the catheter which the biological active substance of this invention is prescribed for the patient throughout an instrument 10, and is used with a chemotherapy in ordinary use -- course **** -- a medicine is not prescribed for the patient by passing through the outside surface which goes via the lumen [like] formed in an instrument 10. Since the biological active substance of this invention is emitted from an instrument 10 needless to say in the lumen formed with this instrument or it is emitted to the organization in contact with an instrument, a lumen can also wear the drugs of some others which should be emitted through here. For example, since the neoplasm which carries out localization into for example, an udder organization or a prostate gland is medicated with tomoxifen SHITORETO, Taxol (trademark) or its derivative, Proscar (trademark), Hytrin (trademark), or Eulexin (trademark), it can apply to the organization exposure side of an instrument.
Dopamine or a dopamine antagonist (for example, bromocriptine mesylate or pel GORAIDO mesylate) is useful for the therapy of neurological diseases, such as a Parkinson Mr. disease. For this object, an instrument 10 can be arranged in vessel supply of the part of thalamus substantia nigra or arbitration so that a therapy may be concentrated in a thalamus.
The biological active substance of other extensive classes can be prescribed for the patient with the instrument 10 of this invention. Therefore, the biological active substance contained in a layer 18 Heparin, covalent-bond heparin or another thrombin inhibitor, hirudine, A leech log, argatroban, D - Phenyl alanyl-L-Polly L-arginyl chloro methyl ketone, Or another anti-thrombon formation medicine or such mixture; Urokinase, Streptokinase, an organization plasminogen activator, or another thrombolysis medicine, or such mixture; -- fibrinolysis medicine; -- vasospasm inhibitor and calcium channel blocker -- The antihypertensive drug; antimicrobial drug or antibiotic of a nitrate, nitrogen oxide, a nitrogen oxide promoter, another vasodilator;Hytrin (trademark), or others; Aspirin, Ticlopidine, glycoprotein IIb/IIIa inhibitor, another inhibitor of a surface glycoprotein acceptor, or another platelet inhibitor; A colchicine, another antimitotic, or another microtubule inhibitor, Dimethyl sulfoxide (DMSO), a retinoid, or another anti-secretion medicine; Cytochalasin or another actin inhibitor; or a RIMODE ring inhibitor; deoxyribonucleic acid, The drugs; methotrexate, another, another antagonism-inhibitor, or another anti-growth medicine for an antisense nucleotide or a molecule heredity break in; Tomoxifen SHITORETO, Taxol (trademark), this derivative, or other anticancer chemotherapeutic drugs; dexamethasone, a dexamethasone-sodium-phosphate salt, dexamethasone acetate, another dexamethasone derivative, another anti-inflammation steroid, or non-steroidal anti-inflammatory drug;
A cyclosporine or another immunosuppressive agent; TORAPIDARU (PDGF antagonist), ANGIOPEPUCHIN (growth hormone antagonist), ANGIO genin, a growth factor, an anti-growth factor antibody, or another growth factor antagonist; Dopamine, The bromocriptine mesylate, the pel GORAIDO mesylate, or another dopamine agonist;60Co (half-life 5.3 years), 192Ir(s) (half-life 73.8 days), 32P (half-life 14.3 days), 111In (half-life 68 hours), 90Y (half-life 64 hours), 99mTc (half-life 6 hours), or another radiotherapy medicine; An iodine content compound, Another heavy metal which functions as a bromine content compound, gold, a tantalum, platinum, a tungsten, or a radiopacity agent; A peptide, Protein, an enzyme, an extracellular stromata

component, a cell component, or another biological drugs; Captopril, Enalapril or another ANGIODENSHIN alteration enzyme (ACE) inhibitor; An ascorbic acid, The alpha-tocopherol, a superoxide dismutase, deferoxamine, 21-amino steroid (Lasa Lloyd), or another free radical scavenging medicine, iron chelating agent or antioxidizing medicine; -- the indicator was carried out with the radioisotope of 14C, 3H, 131I, 32P, or 36S -- or which above drugs; estrogen, another sex hormone;AZT, or others of another form by which the radioisotope indicator was carried out -- anti- -- polymerase; aciclovir -- Famciclovir, a rimantadine hydrochloride, ganciclovir sodium, NORUBIRU, Crixivan, or other antiviral drugs; 5-aminolevulinic acid, A meta-tetra-hydroxyphenyl chlorin, a hexa deca fluoro zinc phthalocyanine, Tetramethyl hematoporphyrin, a rhodamine 123, or another photodynamics remedy ;P A seudomonas aeruginosa exogenous toxin is opposed. A431 EPIDEROMOIDO cancer cell and a reactant IgG2 kappa (kappa) antibody, Remedy; gene therapy medicine aiming at the monoclonal antibody which opposes the noradrenalin enzyme dopamine beta-hydroxylase which carried out covalent bond to saporin, or other antibodies; enalapril and other prodrugs ;P roscar (trademark), Hytrin (trademark), other benign-prostatic-hypertrophy (BHP) remedies or such which mixture; and the small intestine submucosa (SIS) of various configurations, and ** -- at least one is contained.
In the desirable embodiment, a biological active substance layer contains much more preferably per cm2 of the total surface area of the structure, and about 0.01mg - about 10mg of about 0.1mg - about 4mg of biological active substances preferably especially. "The total surface area" means the surface area calculated from most or the whole range of the structure. Therefore, it is not necessary to be the actual surface area of the specific configuration of the structure, or each part. It will be thickness 0 if it puts in another way.
The drugs of per 001 inches and about 100microg - about 300microg within the limits can be contained on an instrument front face.
However, when the structure 12 is formed as vessel stent, especially the desirable matter is the mixture of heparin, anti-inflammation steroids (for example, dexamethasone, its derivative, etc.), and a heparin and such a steroid as a biological active substance of a layer 18.
Drawing 1 is referred to further. The instrument 10 of this invention also has at least one porous layer 20 arranged on the front face which does not contain the layer 18 top of a biological active substance, and a biological active substance. The object of a porous layer 20 is for making it emit at the rate by which the biological active substance was controlled, when the instrument 10 has been arranged in a patient's circulatory system. The thickness of a porous layer 20 is chosen so that the bleedoff rate of such a request may be brought about.
Furthermore, the porous layer 20 is constituted from a polymer preferably vapor-deposited by vacuum deposition on the biological active substance layer 18 by the detail. a this object sake -- plasma vacuum deposition -- being useful . Preferably, a layer 20 is a layer by which the polymerization was carried out from the steam which does not contain a solvent, a catalyst, or the same polymerization promotor at all. Moreover, as for the polymer in a porous layer 20, it is desirable without application of an operation of a curing agent or an operation like heating, a visible ray or ultraviolet rays, a radiation, a supersonic wave, etc. that it is the polymer which carries out a polymerization automatically by the condensation from a vapor phase. As for the polymer in a porous layer 20, it is most desirable that they are polyimide, parylene, or a parylene derivative.
It is thought that the parylene or the parylene derivative vapor-deposited first forms the network structure similar to the fibrous mesh which has a comparatively big hole. furthermore, the hole with which about [that a porous layer 20 becomes thick], parylene, or a parylene derivative was previously formed as it was vapor-deposited -- it is vapor-deposited inside and an existing hole is made small. Therefore, the bleedoff rate of the matter from at least one layer 18 of a biological active substance is controllable to a precision by controlling vacuum evaporationo of parylene or a parylene derivative to accuracy carefully. For this reason, a biological active substance exists in the lower part of at least one porous layer 20 rather rather than the inside of a porous layer 20 or this the whole distributes. However, the biological active substance layer 18 also protects a porous layer 20 during arrangement (it is insertion to a patient's circulatory system or suitable part by the catheter) of an instrument 10.

As shown in drawing 1 , at least one additional enveloping layer 16 arranged between the structure 12 and at least one layer of a biological active substance can also have the instrument 10 of this invention further. Although the additional enveloping layer 16 can also be a mere primer for remedies, as for the additional enveloping layer 16, it is desirable to consist of same polymers as at least one porous layer 20. However, as for the additional enveloping layer 16, it is desirable that it is low porosity, and it is much more more desirable than at least one porous layer 20 that it is nonporosity in general. " -- in general, nonporous" means that it is impermeability, so that it is enough for the additional enveloping layer 16 to prevent the serious interaction between the base material 14 of the structure 12, and the blood with which an instrument 10 is exposed while in use. By the activity of the additional enveloping layer 16 which is nonporosity in general, the activity of the base material 14 poisonous or harmful as mentioned above is enabled.
However, even if the base material 14 of the structure 12 is biocompatibility, it is desirable by using the in general nonporous enveloping layer 16 to isolate a base material 14 from blood.
The polymer systems of others which can be used by this invention are polymers which is the non-gas-like addition polymerization nature ethylene system unsaturated compound which has at least two cross-linking C-C (carbon-carbon) double bonds, has the boiling point 100 degrees C or more and the molecular weight of about 100 to 1500 within the limits with atmospheric pressure preferably, and can generate the amount addition polymer of giant molecules easily and which are guided from a photopolymerization nature monomer which is a liquid monomer. Furthermore, this monomer is the addition photopolymerization nature polyethylene system partial saturation acrylic ester containing two or more the acrylate or the methacrylate radicals per molecule, methacrylic ester, or such mixture preferably. The examples to such polyfunctional acrylate are ethylene-glycol-diacrylate, ethylene glycol dimethacrylate, TORIMECHIRO pro pantry acrylate, TORIMECHIRO propane trimetaacrylate, pentaerythritol tetraacrylate, pentaerythritol tetra-methacrylate, 1, and 6-hexanedioldimethacrylate, diethylene-glycol dimethacrylate, etc.
Especially the examples of a useful monomer are n-butyl acrylate, n-butyl methacrylate, 2-ethylhexyl acrylate, laurylacrylate, 2-hydroxypropyl acrylate, etc. The amide of a little (meta) acrylic acid like N-methylol meta-acrylamide butyl ether is also suitable, and the vinyl ether of the vinyl ester of an N-vinyl compound like N-vinyl pyrrolidone and aliphatic series monocarboxylic acid like oleic acid vinyl, butanediol -1, and diol like 4-divinyl ether, the allyl compound ether, allyl ester, etc. are suitable. The monomer of others like the resultant of G like butane JIRU -1, 4-diglycidyl ether, or bisphenol A diglycidyl ether or poly epoxide, and an acrylic acid (meta) can also be used. By choosing a monomer or monomer mixture suitably, the property of a photopolymerization nature liquid dispersion-medium object is changeable so that it may be suitable for the specific object.
Other useful polymer systems are biocompatibility and are polymers which make min the stimulus to a vessel wall in case the stent is transplanted. Although this polymer can be in any of living body stability or a living body absorption polymer according to a desired bleedoff rate or desired polymer stability, in the embodiment of this invention, its living body absorption polymer is desirable. It is because a living body absorption polymer does not exist over the long period of time after transplantation unlike a living body stability polymer, so the chronic local reaction which does an adverse effect is not caused. An usable living body absorption polymer is Pori (L-lactic acid).
The poly caprolactone, Pori (lactide glycolide), Pori (hydroxy butyrate), Non [Pori (hydroxy butyrate and valerianate) and poly dioxa] Poly ortho ester, a polyacid anhydride, Pori (glycolic acid), Pori (D, L-lactic acid), Pori (a glycolic acid and trimethylene carbonate), phlyphosphate, Phlyphosphate urethane, Pori (amino acid), cyanoacrylate, Pori (trimethylene carbonate), Pori (imino carbonate), They are copoly (ether ester) (for example, PEO/PLA), a polyalkylene OKISA rate, polyphosphazene, biomolecule (for example, a fibrin, a fibrinogen, a cellulose, starch, a collagen, and hyaluronic acid), etc. Moreover, the living body stability polymer which has a comparatively low chronic tissue reaction like polyurethane, silicon, and polyester can also be used. It can be made to dissolve, and by the stent up, if a polymerization can be carried out,

hardening or the polymer which is others can also be used. Such a polymer For example, a polyolefine, polyisobutylene, and ethylene-alpha olefin copolymer; acrylic-acid polymer and a copolymer, A vinyl halogenide polymer and a copolymer (for example, polyvinyl chloride); Polyvinyl ether ; The poly vinylidene halogenide (For example, polyvinyl methyl ether) ; A polyacrylonitrile, (For example, polyvinylidene fluoride and a polyvinylidene chloride) Polyvinyl ketone; Aromatic series polyvinyl (for example, polystyrene), polyvinyl ester ; Between vinyl monomers and a copolymer with an olefin (For example, polyvinyl acetate) for example, an ethylene methyl methacrylate copolymer and an acrylonitrile styrene copolymer -- ABS plastics and an ethylene vinyl acetate copolymer; A polyamide ; Alkyd resin, (For example, Nylon 66 and the poly caprolactam) polycarbonate; -- polyoxymethylene; -- polyimide; -- polyether; -- an epoxy resin -- polyurethane; -- rayon; -- rayon triacetate; -- a cellulose and cellulose acetate -- Cellulose butyrate, cellulose-acetate-butylate; cellophane; cellulose nit rate; cellulose propionate; they are cellulose ether;, a carboxymethyl cellulose, etc.

The other approaches can also be used although plasma vacuum deposition and gaseous-phase vacuum deposition are desirable approaches for making various coats adhere to a stent front face. For example, a polymer solution can be applied to the stent, a solvent can be evaporated, and, thereby, the coat of a polymer and the matter for a therapy can be made to form in a stent front face. A solution can be applied to the stent by spraying this solution on the stent or generally, immersing the stent into a solution. Although it was fundamentally influenced by the viscosity and surface tension of a solution any of a dip painting cloth or fuel-spray spreading it chooses they are, it was discovered that the coverage of the coating which fuel-spray spreading by detailed atomiser like a commercial airbrush forms the coat which has the highest homogeneity, and should be applied to the stent is strictly controllable.

Also in the coat applied by the fuel spray or which approach of immersion, in order to acquire the outstanding coat homogeneity and a controllability with the strict amount of the matter for a therapy applied to the stent, generally it is desirable to perform two or more spreading processes.

When the layer 18 of a biological active substance contains comparatively soluble matter like heparin, and when at least one porous layer 20 consists of parylene or a parylene derivative, as for the thickness of at least one porous layer 20, it is desirable that it is within the limits of about 5,000 to 250,000 A, its within the limits of about 5,000 to 100,000 A is much more desirable, and its about 50,000 A is the most desirable. When at least one additional enveloping layer 16 consists of parylene or a parylene derivative, as for the thickness of at least one additional enveloping layer 16, it is desirable that it is within the limits of about 50,000 to 500,000 A, its within the limits of about 100,000 to 500,000 A is much more desirable, and its about 200,000 A is the most desirable.

When at least one layer 18 of a biological active substance contains comparatively soluble matter like heparin, the thing of the total surface area of the structure 12 for which at least one layer 18 contains per two and about 0.1-4mg of biological active substances in a total amount 1cm is desirable. the bottom of the typical blood flow which minds the vessel stent with these loadings -- per day -- desirable -- 0.1 - 0.5 mg/cm2 -- the heparin bleedoff rate (measured value in a test tube) of about 0.25 mg/cm2 is brought about preferably. The solubility of dexamethasone can be adjusted as a request, without [which adds heparin] depending especially or adding. For example, heparin can be adjusted by mixing one or more kinds of comparatively soluble derivatives like a dexamethasone-sodium-phosphate salt.

Drawing 11 shows the instrument 10 of another embodiment of this invention with which the enveloping layer 16 is directly applied to the outside surface of the base material 14 of the structure 12. As for an enveloping layer 16, with this configuration, it is desirable that they are the above nonporous enveloping layers. When an enveloping layer 16 consists of a parylene derivative, as for the thickness of the nonporous enveloping layer 16, it is desirable that it is within the limits of about 50,000 to 500,000 A, its within the limits of about 100,000 to 500,000 A is much more desirable, and its about 200,000 A is the most desirable. In this embodiment of this invention, the nonporous enveloping layer 16 can also be an adsorbent. It is defined as an adsorbent as drugs which draw other matter or particles on the front face as shown in Dorland's

Illustrated Medical Dictionaey 26th Edition by W.B.Saunders Co., Philadelphia, and PA. Then, the biological active substance 18 is combined with the front face of an enveloping layer 16. the additional enveloping layer 20 -- a biological active substance -- the total -- it can apply to the top face of 18. As an exception method, a coating layer and identitas, or a different biological active substance can also be applied to the front face of the biological active substance layer 18 by turns. However, in this special embodiment of this invention, the outside surface of the structure 12 is the biological active substance layer 18.

In the another embodiment of this invention as shown in drawing 11 , it can be considered that an enveloping layer 16 is the adsorption layer and/or absorption layer with which the biological active substance was combined.

As an example, an instrument 10 is the stainless-steel GR II (trademark) stent. In this case, as for the stainless-steel base material 14 of the structure 12, a polymer, especially parylene are applied. The thickness of the adsorption polymer layer 16 of this parylene is about 230,000A. The biological active substance layer 18 of an anti-platelet GP IIb/IIIa antibody (AZI) is passively added on the adsorption polymer layer 16. About the polymer coat stainless-steel stent, it is the buffer water solution (1mg [ml] /, pH=7.2) of AZ1 37-degree C antibody.

You made it immersed for **** 24 hours. AZ1 is a monoclonal anti-rabbit platelet glycoprotein (GP) IIb/IIIa antibody. It was checked by activity soot ****** in AZ1 by which the indicator was carried out with radioisotope that the antibody of surface area about 0.02microg (it is about 2microg in a total amount in the case of the 3x20mm GR II (trademark) stent) of the stent had been added. [of 1mm] [per two] Moreover, in the floating system in a test tube (PBS solution of 10 ml/min and 1%BSA), it was also checked that the abbreviation moiety of the antibody added by the stent also after the perfusion for about ten days had remained.

It is thought that the device in which a drug is added by the stent is based on adsorption on the front face of a polymer layer and/or the absorption to a polymer.

In the precedence research on the same addition and the bleedoff of AZ1 to the cellulose coat stainless-steel stent, inhibition of platelet aggregation and lowering of a thrombosis rate were accepted in the depths arterial injury model by the rabbit. (Aggarwal et al., Antithrombotic Potential of Polymer-Coated Stent Eluting Platelet Glycoprote in IIb/IIIa Receptor Antibody, American Heart Association Circulation Vol.94, No.12, December 15, 1996, 3311 to pp3317 reference.)

In the another example, c7E3 Fab was combined with the polymer enveloping layer 16 as a biological active substance layer 18. Biological active substance c7E3 Fab is a chimera monoclonal antibody which acts on the GP IIb/IIIa integrin on a platelet, in order to prevent condensation of a platelet. This antibody or an acceptor blocker can be used within a human vein, in order to prevent the thrombosis in a coronary artery angioplasty. This acceptor blocker is known also as ReoPro (trademark) marketed from Eli Lilly, Indianapolis, and IN. The biological active substance layer 18 of an anti-platelet GP IIb/IIIa antibody (c7E3 Fab) is passively added by the adsorption polymer layer 16. The polymer coat stainless-steel stent was made immersed in the buffer water solution (1mg [ml] /, pH=7.2) of a 37-degree C c7E3 Fab antibody for about 24 hours. c7E3 Fab is inhibitor of a human platelet plug. It was checked by activity soot ****** in c7E3 Fab by which the indicator was carried out with radioisotope that the antibody of surface area about 0.010microg (it is about 10microg in a total amount in the case of the 3x20mm GR II (trademark) stent) of the stent had been added. [of 1mm] [per two] Moreover, in the floating system in a test tube (PBS solution of 10 ml/min and 1%BSA), it was also checked that the abbreviation moiety of the antibody added by the stent also after the perfusion for about ten days had remained.

Drawing 12 is the sectional view of another embodiment of the instrument 10 of drawing 11 . In this embodiment, the parylene adhesion acceleration layer 30 is first applied to the stainless-steel base material 14 of the structure 12. for example, the adhesion acceleration layer 30 -- thickness -- for example, 0.5-5,000A -- it is the thin film of the silane of 2-50A within the limits preferably. As for this silane adhesion acceleration layer, it is desirable that it is A-174 silane containing nu-methacryloxypropyltrimethoxysilane. This is marketed from Specialty Coating Systems Inc., Indianapolis, and IN. When forming the outside surface of a base material 14, this

outside surface is first defecated by isopropyl alcohol. subsequently, the stent -- the inside of a silane -- being immersed -- the outside surface of a base material -- **** of a silane -- the thin film is applied. The another formation approaches of the outside surface of a base material 14 are plasma etching, grit blast finish, etc. The formation approach consists of defecating the outside surface of a base material by isopropyl alcohol first, carrying out plasma etching of the outside surface of a base material, and applying a silane to the front face by which plasma etching was carried out. In grit blast finish, grit blast finish of the outside surface of a base material is carried out, subsequently, the outside surface of a base material is defecated by isopropyl alcohol, and a silane is applied to this defecated grit blast finished surface.
As shown in drawing 2 , the instrument 10 of this invention is not limited only to inclusion of the monolayer 18 of a biological active substance. For example, an instrument 10 can have the 2nd layer 22 of the biological active substance arranged on the structure 12. If it does not even say that the 2nd layer is arranged without the medium porous layer 24 with the 1st layer in the same field of an instrument 10, although the biological active substance of 22 is not necessarily required, it can differ from the biological active substance of the 1st biological active substance layer 18 the 2nd layer. By using a biological active substance which is different in a layer 18 and a layer 22, an instrument 10 can achieve two or more therapy functions.
The instrument 10 of this invention can have further the additional porous layer 24 of the polymer arranged between the layer 18 of a biological active substance, and a layer 22. Although repeated, the biological active substance 18 exists on one field of the structure 12. The field of another side cannot have a biological active substance, either, or can also have one or more kinds of different biological active substances. The additional porous layer 24 can make the biological active substance in a layer 18 and a layer 22 emit at a different bleedoff rate.
Simultaneous, as an exception method, **** 10 differ mutually and can also use two or more biological active substances which have different solubility in two layers 18 and a layer 22. In such a case, it is convenient to arrange the layer 22 which contains the biological active substance of low solubility on the layer 18 containing the biological active substance of high solubility, and, moreover, it is desirable. The biological active substance 18 can also be made to contain as an exception method, in inside, such as a hole generated in a stent front face, a hollow, and a slot, as shown in drawing 8 -10. This is further explained to a detail in the following.

For example, when the structure 12 of an instrument 10 is formed as vessel stent, at least one layer 18 contains the heparin of high solubility comparatively, and, as for the 2nd layer 22, it is convenient to contain the dexamethasone of low solubility comparatively.
Without expecting, heparin promotes bleedoff of dexamethasone and brings about a high dexamethasone bleedoff rate numbers of times rather than the dexamethasone bleedoff rate when not using heparin. Although the bleedoff rate of heparin also falls, extent of lowering is not so dramatic if compared with buildup of a dexamethasone bleedoff rate. Furthermore, in a detail, when dexamethasone itself is arranged by the lower part of the porous layer 20 which has the above dimensions, the bleedoff rate can be disregarded. Only when the thickness of a porous layer 20 falls or less to 1/10, a proper bleedoff rate is obtained. On the other hand, when the layer 22 of dexamethasone is on the layer 18 of heparin and is arranged by the lower part of the porosity parylene layer 20, dexamethasone can be made to emit at the rate of the request of an about 1-10microg/cm2/day. Furthermore, it is thought that it is maintained even after, as for this high bleedoff rate of dexamethasone, all heparin is emitted from a layer 18, without expecting at all.
The biological active substance layer 18 and/or 22 are applied to an instrument 10 regardless of a porous layer 20 and/or spreading of 24. Before inserting an instrument 10 in a patient's circulatory system, a layer 18 and/or the biological active substance from 22 do not expect mixing to a porous layer 20 and/or 24, and are mere chance. The bleedoff rate of a biological active substance is further controllable by this phenomenon from the case where a polymer layer is made to only distribute a biological active substance, to accuracy.
An instrument 10 does not need to have the additional porous layer 24, when the biological active substance layers 18 and 22 more than two-layer exist. As shown in drawing 3 , a layer 18

and a layer 22 can also be directly inserted, while it is mutual, although it does not need to be separated by the porous layer. It is desirable to arrange the layer 22 which contains the biological active substance of low solubility comparatively also in this embodiment on the layer 18 which contains the biological active substance of high solubility comparatively.
Irrespective of existence of the additional porous layer 24 or un-existing, the thing of the total surface area of the structure 12 for which layers 18 and 22 contain per two, heparin, and about 0.05-2.0mg of dexamethasones 1cm, respectively is desirable. Therefore, as for the total amount of the biological active substance arranged in the layer 18 on the structure 12, and 22, it is desirable that it is within the limits of about 0.1 to 10 mg/cm2.
Some dexamethasone derivatives like a dexamethasone-sodium-phosphate salt have solubility in general higher than the dexamethasone itself. When a high solubility dexamethasone derivative is used as a biological active substance in the instrument 10 of this invention, the thickness of at least one porous layer 20 (and additional porous layer 20) must be adjusted according to this.
The above specific structures of an instrument 10 can be fitted to a specific application by various approaches. For example, an instrument 10 can also have further the same or a different layer of a biological active substance. An additional porous layer can also be made to separate or it is not necessary to make the additional layer of these biological active substances separate by request for convenience. As an exception method, an additional porous layer can also separate only some additional biological active substance layers. Furthermore, one biological active substance can be arranged into a certain part of the structure 12 of an instrument 10, and another biological active substance can be arranged into another part of the structure 12 of an instrument 10.
As an exception method, completely have the additional enveloping layer 16 and an instrument 10 may not be. Such structure is shown in drawing 4 . In drawing 4 , the biological active substance 18 is arranged directly on the top face of the base material 14 of the structure 12. In such a case, especially the thing for which surface treatment of a base material 14 or surface activity-ization is performed, and adhesion or adhesion of a biological active substance of a up to [a base material 14] is especially promoted before at least one adhesion of a porous layer 20 is desirable. Surface treatment and surface-activity-izing can also make the bleedoff rate of a biological active substance change selectively. Such processing can be used also in order to promote adhesion at the additional enveloping layer 16 (if it exists) to a base material 14 top, or adhesion. Additional enveloping layer 16 the very thing, the 2nd, or additional porous layer 24 the very thing can be similarly processed, in order to promote adhesion or adhesion of the biological active substance layer 18, or in order to control the bleedoff rate of a biological active substance further.
The useful approach of surface preparation can include any of the various approaches, such as the chemical denaturation of physical denaturation; of defecation; etching, perforation, a cut, or polish and solvent processing, spreading of undercoat, spreading of a surface active agent, plasma treatment, an ion bombardment, covalent bond, etc., they are.
It was discovered that especially the thing to do for the plasma treatment of the additional enveloping layer 16 which consists of parylene before making the biological active substance layer 18 adhere to the top face of the additional enveloping layer 16 is useful. Plasma treatment heightens the adhesive strength of a biological active substance, can increase the amount of the biological active substance which can be made to adhere, and can make a biological active substance deposit in the shape of [much more uniform] a layer. It is dramatically difficult to make hygroscopic drugs like heparin actually adhere to the native parylene front face of a difficulty wettability in hydrophobicity. However, by plasma treatment, a parylene front face is made into a wettability and it makes it possible to make heparin adhere to a parylene front face easily.
Surface treatment is carried out by which the aforementioned approach, the bleedoff rate of a biological active substance is changed, and/or neither of porous layers 20 and 24 is so, and it can make the biocompatibility of the front face of a layer improve. For example, the front face of these layers is further made into haemocompatibility by applying to a layer 20 and/or 24 polyethylene oxide, a phosphatidyl chlorin, or finishing of a biological active substance (for

example, heparin which carried out covalent bond) that carried out covalent bond. Similarly, by spreading of a layer 20 and/or the plasma treatment to 24, or a hydrogel coating, surface energy can be changed, preferably, the surface energy of 20 - 30 dyne/cm within the limits can be brought about, and, thereby, these front faces can be further made into biocompatibility.
Drawing 5 is referred to. Drawing 5 shows the embodiment of the instrument 10 with which mechanical association or a connector 26 is arranged between either one layer of the (a) porous layers 20 and 24, the porous layers 20 and 24 of (b) another side, the additional enveloping layer 16 and the base material 14 and all. A connector 26 fixes layers 16 and 20 and/or 24 to a base material 14 firmly mutually. Especially the connector 26 gives the structural integrity to an instrument 10, after the biological active substance layer 18 and/or 20 are all emitted to the patient inside of the body.
For simplification, the connector 26 is illustrated by drawing 5 as two or more projections of a base material 14 which make the single porous layer 20 fix to a base material 14. A connector 26 can be extended from a porous layer 20 by turns to a base material 14 through the biological active substance layer 18. In any case, it is divided into some areas by the connector 26, and the monolayer 18 of a biological active substance is arranged between a porous layer 20 and a base material 14.
A connector can also demonstrate the function to divide a different biological active substance to the field where instrument front faces differ.
A connector 26 can be arranged by various approaches. For example, a connector 26 can be formed as a single piece to a base material 14, in case the structure 12 is formed or cast first. As an exception method, a connector 26 can also be formed as separate elements, such as the pons and stanchion which are added to the existing structure 12, a pin, or a stud. Moreover, a connector 26 can also be formed as a **** land, a shoulder, a plateau, a pod; or a dished depressed ground on a base material 14 etc. As an exception method, some base materials 14 between the desirable locations of two or more connectors 26 can be removed by approaches, such as etching and mechanical polishing, and the biological active substance layer 18 can also be arranged among these. or [that a connector 26 wipes a part of biological active substance layer 18 applied previously] -- or it can form so that it may extend downward toward a base material 14, and the nakedness part of a base material 14 can also be made to arrange a porous layer 20 by direct-vapor-deposited or plasma vapor-depositing by carrying out etching clearance The approach of others to which some base materials 14 are exposed for the direct continuation to a porous layer 20 is common knowledge at this contractor.
In the another desirable embodiment as shown in drawing 6 A, drawing 6 B, and drawing 7 , the biological active substance 18 is arranged on one front face of the base material 14 which constitutes the structure 12 in drawing 6 A. Drawing 7 shows the flatness before being made a coiled form, or the stent 10 of a flat-surface condition. The porous layer 20 applied to the outermost side of the stent 10 is illustrated by drawing 7 . Drawing 6 A and drawing 6 B are the sectional views which met six to 6 line of drawing 7 . In drawing 6 A, the biological active substances 18 arranged on one front face of a base material 14 are various different remedies and/or diagnostic drugs. For example, an instrument 10 is stent arranged to a patient's inside of the body, in order to prescribe a chemotherapic drug like tomoxifen SHITORETO or Taxol (trademark) for the patient near a neoplasm or to medicate a neoplasm directly. A porous layer 20 enables bleedoff controlled by the accuracy of the biological active substance 18 while it is arranged on the biological active substance 18 and forms a smooth side. Furthermore, as shown in drawing 6 A, covalent bond for example, of heparin 18' is carried out to the field of the opposite hand of an instrument 10 to the porous layer 20. In order to bring about an anti-thrombus operation and haemocompatibility especially, as for this field, it is desirable to face the lumen of a blood vessel. As mentioned above, the 3rd different biological active substance (not shown) can be arranged on the 1st biological active substance 18 and the base material 14 of an opposite hand, and to the same covalent-bond heparin or base material 14 side as other biological active substances (for example, other covalent-bond biological active substances), and a porous layer 20 can also separate.
The modification of the embodiment shown in drawing 6 A is shown in drawing 6 B. In drawing 6

B, two kinds of biological active substances 18 and 18' are arranged on the same field of the base material 14 of the structure 12. The porous layer 20 is arranged on the biological active substance non-existed side of the base material 14 besides the biological active substance 18 and 18'. This embodiment shows a case it is desirable to medicate with two kinds of drugs (for example, a chemotherapic drug and an antivirotic) the body tissue to which the specific field of an instrument 10 is exposed. Furthermore, the reverse side of the instrument with which a biological active substance does not exist can be used for arranging one or more kinds of biological active substances or remedies (for example, antithrombotic drug).
As mentioned above, two or more biological active substances and porous layers can be applied to an instrument 10. In this case, limit elements are the whole instrument thickness, the adhesive strength of two or more layers, etc.
In the still more nearly another embodiment of this invention, the instrument of this invention possesses opening for containing a biological active substance in an instrument. This embodiment is illustrated by drawing 8 , drawing 9 , and drawing 10 A, drawing 10 B, drawing 10 C, and drawing 10 D. Drawing 8 shows the arm of the stent of drawing 7 . this arm -- a hole 28 -- having -- a biological active substance -- this hole -- it contains inside. Drawing 9 shows the cross section of the stent which met nine to 9 line of drawing 8 . The biological active substance 18 is contained in a hole 28. In this case, a base material 14 has an enveloping layer 16, and a porous layer 20 forms the outermost layer of drum for diffusing a biological active substance through this layer further. In the another embodiment, hole 28' which can make the biological active substance 18 contain can be cut, etched or die pressing fabricated in a base material 14. This embodiment is illustrated by drawing 10 A, drawing 10 B, drawing 10 C, and drawing 10 D. These drawings are sectional views which met ten to 10 line of drawing 8 . Hole 28' can also take the configuration of the slot prepared in the front face of the base material 14 of a medical device, or a slot. If hole 28' is made into such a configuration, the effectiveness that the bleedoff rate besides the whole quantity of the biological active substance 18 which should be emitted is further controllable to accuracy will be acquired. for example, -- drawing 10 -- D -- being shown -- having -- as -- V -- a typeface -- a hole -- 28 -- ' -- being little -- biological -- an active substance -- **** -- it cannot contain -- moreover -- drawing 10 -- B -- being shown -- having -- as -- much more -- being uniform -- linear -- bleedoff -- a rate -- having -- a rectangle -- ** -- a hole -- 28 -- ' -- comparing -- a geometric rate -- a biological active substance -- emitting .
The aforementioned hole, a hole, a slot, a slot, etc. can be made to form into the structure of an instrument 10 with various means. For example, such a means is the approach of reaching [which uses punching which consists of using laser, electron beam machining etc., a cut, or a photoresist processing approach], and etching desired opening.
They can be used making all the biological active substances of the above which can be applied to the front face of an instrument 10 able to include in opening in these embodiments of this invention. The outside surface of an instrument can also be made to apply and **** a biological active substance layer and a porous layer, as similarly heparin was explained to one field of the instrument shown in drawing 9 above about other embodiments of this invention that covalent bond can be carried out.
He could understand the manufacture approach of the instrument 10 by this invention by the aforementioned explanation. In the easiest form, the approach of this invention makes at least one layer of a biological active substance adhere on the structure 12, then consists of making at least one porous layer 20 adhere by vacuum evaporationo or plasma vacuum evaporationo preferably on at least one biological active substance layer 18 on one field of the structure 12. At least one porous layer 20 consists of biocompatibility polymers, and it has the thickness suitable for emitting at the rate by which the biological active substance was controlled. Preferably, at least one additional enveloping layer 16 is first arranged on the base material 14 of the structure 12 by vapor-depositing directly. Such vacuum evaporationo generates or receives G para xylene or its derivative, sublimates or pyrolyzes this G para xylene or its derivative, and generates the para xylene or the monomer derivative of a monomer, and this monomer is simultaneously performed condensation and by carrying out a polymerization on a base material

14. A vacuum evaporationo process is performed in a vacuum. As for the inside of a vacuum evaporationo process, a base material 14 is maintained by the temperature a room temperature or near a room temperature. Vacuum evaporationo is under the solvent for a polymer, or un-existing [of a catalyst], and it is performed, without using any operations for promoting a polymerization. An example of a suitable derivative to carry out this vacuum evaporationo process is dichloro-para xylene. In order to form an enveloping layer 16, as for parylene or a parylene derivative, being applied by the above thickness is desirable. Although this enveloping layer 16 is nonporosity in general, it is low **** from at least one porous layer 20 to which it is applied in any case. When needed by the presentation of an enveloping layer 16, surface treatment of the layer 16 is carried out by suitable approaches, such as the above plasma treatment, for example.

Subsequently, at least one layer 18 of a desired biological active substance is especially applied to one field of the structure 12 on an additional enveloping layer. This spreading process can be carried out using the approach of various daily use. For example, the liquid mixture of a biological active substance is applied on the additional enveloping layer 16 by immersion coating, roll coating, brush coating, or fuel-spray coating, or electrostatic adhesion of the liquid mixture or desiccation mixture of a biological active substance can be carried out, or it can apply by the other suitable approaches. A different biological active substance can also be applied to the area or field where instruments differ.

Especially the thing for which the mixture of a biological active substance and volatile fluid is applied to the structure, and volatile fluid is subsequently removed by the suitable approach (for example, the approach of making it evaporate etc.) is convenient. When heparin and/or dexamethasone, or its derivative is used as a biological active substance, volatile fluid is ethyl alcohol preferably. As for a biological active substance, being applied in the above amount is desirable.

The approach of others which make the biological active substance layer 18 adhere on the structure 12 is also equally useful. However, I hear that the biological active substance must be held physically, and it has it in a proper place that it is important irrespective of the method of application until it adheres to a porous layer 20 on a biological active substance layer. Thereby, in order to hold a biological active substance on other instruments, the activity of the suitable approach of the support and the surfactant which are often used, chemical bond material, or others etc. is avoidable. An additive or an approach changes a biological active substance, or the additive used by such approach has a poisonous thing, and it may make it deteriorate and reduces the validity as a result, and in being still severer, itself is sometimes poisonous. Since the biological active substance layer 18 of this invention is adhered by request in spite of it, the approach of these others can also be used.

A biological active substance can also be made to adhere as a particle layer as a smooth layer on one field of the structure 12 needless to say. Furthermore, it can also be made to adhere so that the biological active substance with which the fields where instruments differ differ the biological active substance with which plurality differs may be contained. In the case of the latter, particle size may affect the engine performance or properties of an instrument 10, such as the homogeneity of the adhesive strength of the upheaval in the surface area in which it adheres to the profile of the smooth nature of the topmost porosity coat 20, and an instrument 10, and a biological active substance, the bleedoff rate of a biological active substance, and the biological active substance layer 18 or irregularity formation, and the biological active substance layer 18, and reinforcement. For example, it is useful to use the pulverized biological active substance, i.e., the biological active substance with which processing processing of the diameter was generally carried out even at a minute particle size of less than 10 micrometers. However, a biological active substance can also be made to adhere as adsorbent or an absorber to a minute capsulation particle, liposome dispersion liquid, and a minute support particle etc.

In the still more nearly another embodiment by this invention, a biological active substance can also be arranged on one field of the structure 12 by the specific geometrical pattern. For example, a biological active substance is not applied to the head or arm of the stent, a biological active substance is applied along with an parallel line, especially two or more kinds of biological

active substances can also be applied to the same front face.
make it any -- if it adheres to the biological active substance layer 18 in a proper place, at least one porous layer 20 will be applied on at least one biological active substance layer 18 after that by the same approach as the method of application of at least one additional enveloping layer 16. However, a polymer like parylene or a parylene derivative is applied by the above thin thickness, in order to form at least one porous layer 20.
It is suitable sequence and the 2nd biological active substance layer 22 or the layer of others like the additional porous layer 24 is applied by the same approach as the aforementioned approach. As for each process of this approach, it is desirable to carry out using the above biological active substances, the structure, and a base material.
vapor-depositing polyimide by the same approach as said approach carried out about parylene and its parylene derivative needless to say -- a porous layer and the additional enveloping layers 20 and 24, and/or any of 16 -- or all can be supposed and it can also be made to adhere The technique which carries out the plasma vacuum evaporationo of the polymer of a polymer like Pori (ethylene oxide), Pori (ethylene glycol), and Pori (propylene oxide), silicon or methane, tetrafluoroethylene, or tetramethyl disiloxane on other bodies is common knowledge, and these techniques are useful although this invention is carried out.
The option which controls the bleedoff rate of a biological active substance consists of making a monodisperse polymer particle (that is, called a polo gene (porogen)) adhere, before making a porous layer 20 adhere on the front face of the instrument 10 which consists of one or more kinds of biological active substances. After making it make adhere a porous layer 20 and harden, carry out dissolution clearance of the polo gene with a suitable solvent, a cavity or a hole is made to save in an outside enveloping layer, and passage of a lower biological active substance is promoted.
In case Homo sapiens or the patient of a brute is treated medically, he can understand similarly the approach of using the instrument 10 of this invention easily. The approach of this invention is superior to the conventional approach. The approach of this invention consists of inserting the implantable vessel instrument 10 in a patient's inside of the body. This instrument 10 consists of the structure 12 suitable for inserting in a patient's circulatory system. This structure 12 consists of base materials 14. The approach by this invention has the reserve process which consists of making at least one layer 18 of a biological active substance adhere on one field of the structure, then making at least one porous layer 20 adhere on at least one biological active substance layer 18. When this porous layer 20 consists of a polymer and the instrument 10 has been arranged in a patient's circulatory system, it has the thickness suitable for emitting at the rate by which the biological active substance was controlled.
The approach of this invention is accompanied by operation of two kinds of adhesion processes about various embodiments of the above instruments 10 according to the manufacture approach of the further aforementioned instrument 10. Furthermore, the adhesion process of at least one porous layer 20 can include in a detail the process which carries out the polymerization of at least one layer 20 preferably from the steam of a monomer (monomer) steam, the parylene which does not contain a solvent or a catalyst, or a parylene derivative. This approach can also include the process which adheres at least one additional enveloping layer 16 between the structure 12 and at least one biological active substance layer 18 again.
The therapy approach by this invention is completed by inserting an instrument 10 into a patient's circulatory system. At least one porous layer 20 and the additional porous layer 24 of arbitration are the rates controlled to a patient's inside of the body, and emit a biological active substance automatically.
the remaining details of the medical therapy approach worry the details which indicated the manufacture approach of the instrument 10 of this invention, and come out. Therefore, there is no need of explaining these details here repeatedly for simplification.
If the aforementioned explanation is taken into consideration, it will be in ** to offer the implantable medical device which can succeed in control with this invention exact about bleedoff of one or more kinds of biological active substances contained in an instrument. Furthermore, the polymer layers 16 and 20 of polyimide, parylene, a parylene derivative, or others and/or 24

can be made very thin compared with required thickness about other polymer layers. Therefore, the great portion of overall the great portion of [a body or] on the structure 12 can consist of a biological active substance. The thing which exceed by this the amount prescribed for the patient with the conventional instrument and for which a patient is comparatively medicated with the biological active substance of a large quantity becomes possible. Although the part where a patient's inside of the body is various can be medicated with the biological active substance of these large quantities during activation of a medical operation, or after activation, especially although burst nature closeout and/or the restenosis of a blood vessel are prevented, it is useful by medicating with an antithrombotic drug or other drugs the blood vessel part opened by PTA. The bleedoff rate of a biological active substance is carefully controllable by this invention about a short period of time and prolonged both sides. The most important thing is that disassembly of a biological active substance which may take place with other polymer coat techniques is avoided.

As long as it has the reinforcement and flexibility which need various elements with which this invention was indicated in order to carry out, as indicated, indispensable requirements for the detail of the configuration of these elements and others of revival to attain the effectiveness of this invention are considered not to become. It is thought that selection of the details of others of these elements and a configuration will be within the limits of this contractor's capacity if the publication of this description is taken into consideration.

[Translation done.]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DRAWINGS

[Drawing 1]

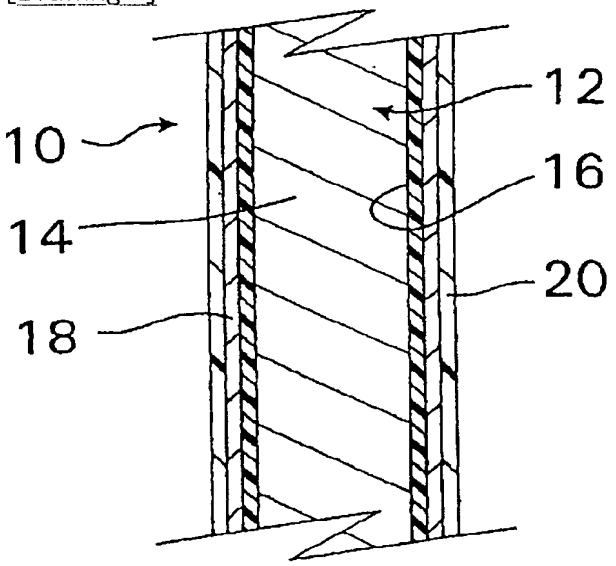

Fig.1

[Drawing 2]

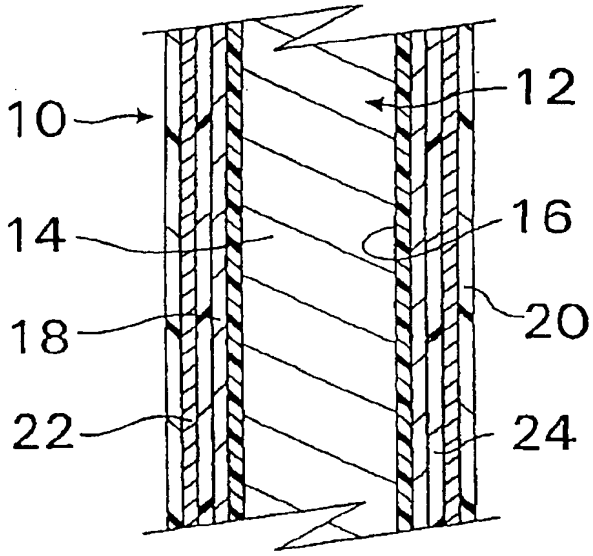

Fig.2

[Drawing 3]

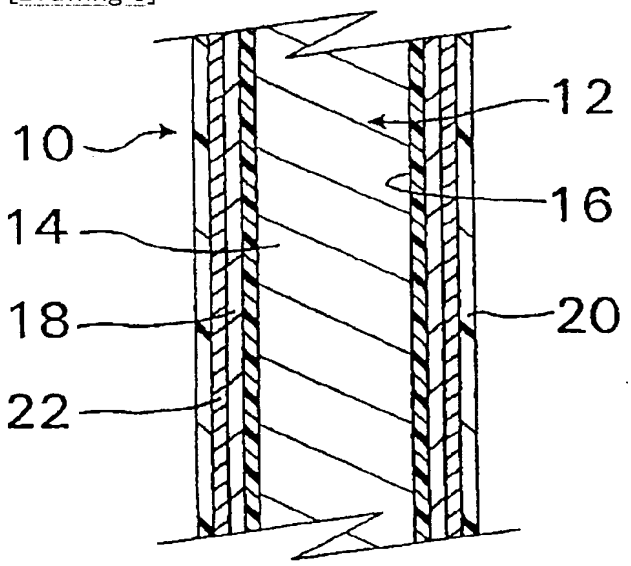

Fig.3

[Drawing 4]

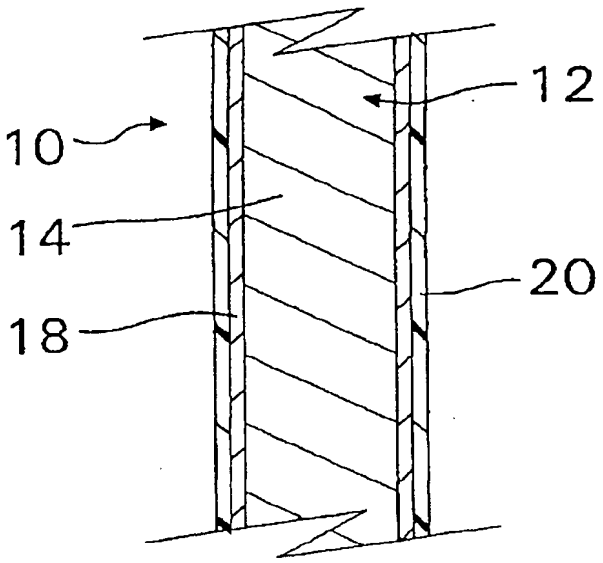

Fig.4

[Drawing 5]

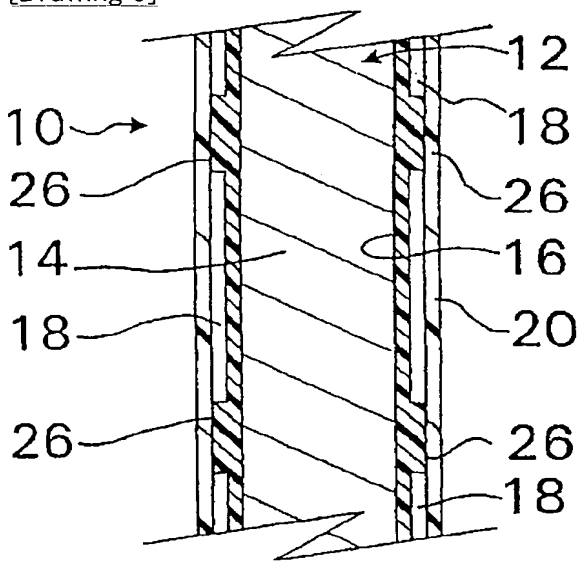

Fig.5

[Drawing 6]

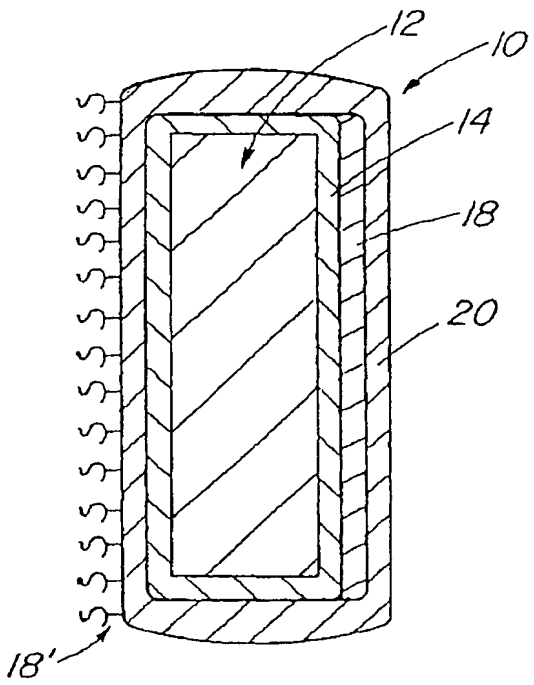

FIG. 6A

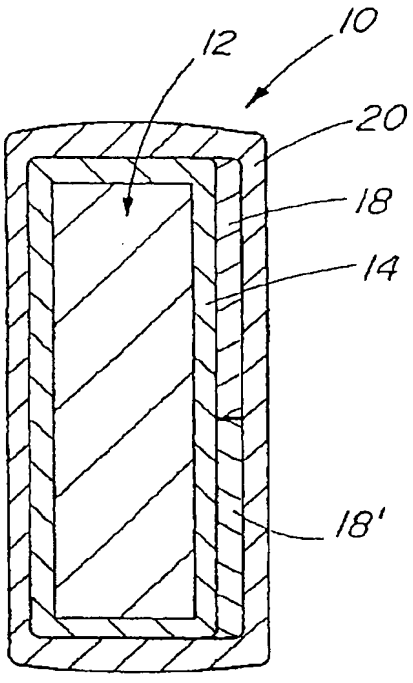

FIG. 6B

[Drawing 7]

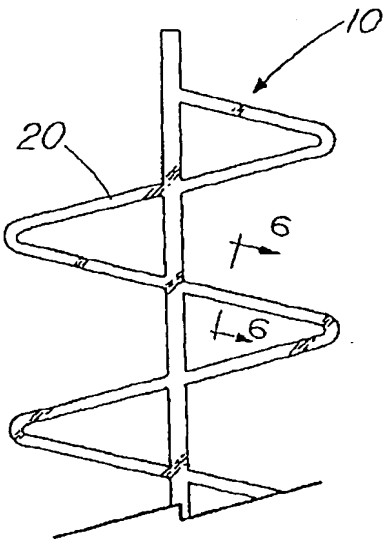

FIG. 7

[Drawing 8]

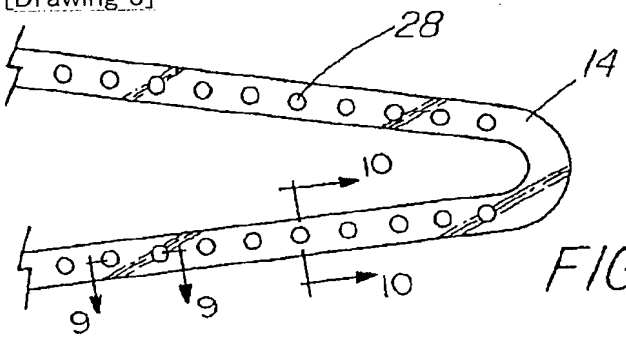

FIG. 8

[Drawing 9]

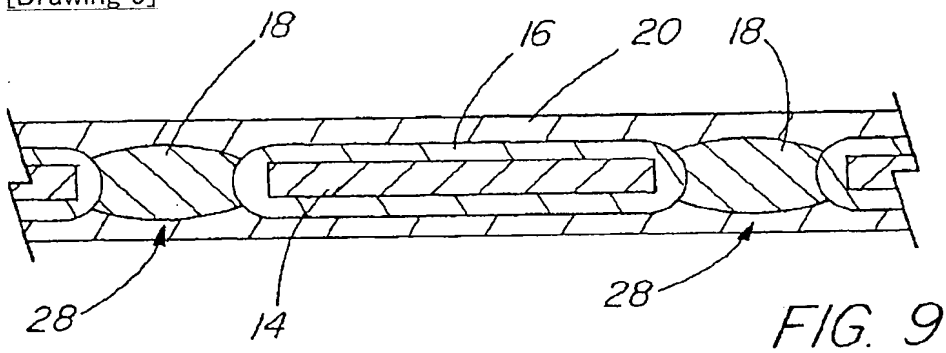

FIG. 9

[Drawing 10]

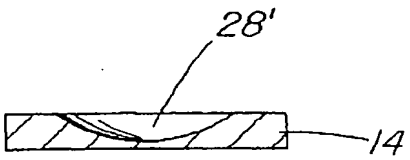

FIG. 10A

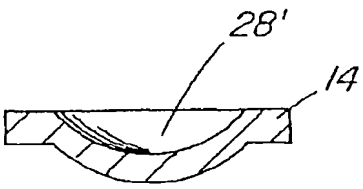

FIG. 10C

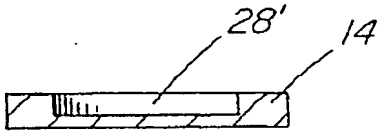

FIG. 10B

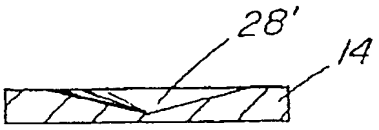

FIG. 10D

[Drawing 11]

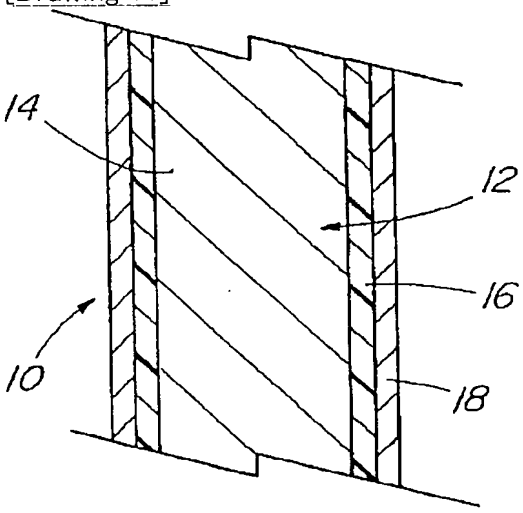

FIG. 11

[Drawing 12]

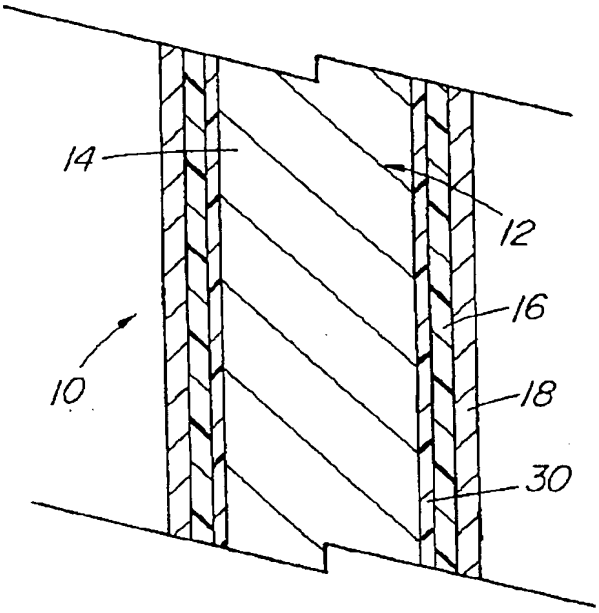

FIG. 12

[Translation done.]